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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/516,072	12/21/2005	Toshihide Kobayashi	P26337	9668

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EXAMINER	
MARTIN, PAUL C	
ART UNIT	**PAPER NUMBER**
1657	

NOTIFICATION DATE	DELIVERY MODE
01/04/2008	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)	
	10/516,072	KOBAYASHI ET AL.	
	Examiner	Art Unit	
	Paul C. Martin	1657	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 October 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *10/12/07* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *3,4,9-11,14,15 and 18-21* is/are rejected.

7)☒ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *12 October 2007* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *10/12/07*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 3, 4, 9-11, 14, 15 and 18-21 are pending in this application and were examined on their merits.

The drawings were received on 10/12/07. These drawings are accepted.

The objection to the Specification for lacking proper citation of Continuity data and for the Brief Description of the Drawings for minor informalities has been withdrawn due to the Applicant's amendments to the Specification filed 10/12/07.

The rejection of Claims 1 and 4 under 35 U.S.C. § 112, 2nd paragraph for lacking specific definition of the term "affinity" has been withdrawn due to the Applicant's amendments to the Specification filed 10/12/07.

The rejection of pending Claims 3, 4, 9-11, 14, 15 and 18-21 under 35 U.S.C. § 112, 2nd paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicant regards as the invention has been withdrawn due to the Applicant's amendments to the Claims filed 10/12/07.

The rejection of pending Claims 1, 3, 4, 9-11, 14, 15 and 19-21 under 35 U.S.C. § 102(b) as being anticipated by Baba *et al.* (2001) has been withdrawn due to the Applicant's amendments to the Specification filed 10/12/07.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 3, 4, 9-11, 14, 15, 18, 19 and 20 are newly rejected under 35 U.S.C. 103(a) as being unpatentable over Baba *et al.* (2001).

Baba *et al.* teaches an *in vitro* method wherein living cells were contacted with PEG-Chol labeled with the affinity substance biotin (bPEG-Chol), followed by incubation with streptavidin-AlexaFluor 488 (fluorescent), the quantitative determination of the amount of bound bPEG-Chol (Pg. 509, Column 1, Lines 15-34) and the qualitative detection of bPEG-Chol binding to cells (Pg. 503, Fig. 2).

Baba *et al.* further teaches the use of PEG-Chol in concentrations of 2.5μM (Pg. 506, Fig. 5).

It is inherent in the method of Baba *et al.* that the bPEG-Chol was detectably labeling cell membrane cholesterol, and thereby also inherently determining the presence and distribution of the labeled bPEG-Chol bound to cholesterol.

The MPEP states:

> "[T]he discovery of a previously unappreciated property of a prior art composition, or of a scientific explanation for the prior art's functioning, does not render the old composition patentably new to the discoverer." *Atlas Powder Co. v. Ireco Inc.*, 190 F.3d 1342, 1347, 51 USPQ2d 1943, 1947 (Fed. Cir. 1999). Thus the claiming of a new use, new function or unknown property which is inherently present in the prior art does not necessarily make the claim patentable. *In re Best*, 562 F.2d 1252, 1254, 195 USPQ 430, 433 (CCPA 1977).
>
> The discovery of a new use for an old structure based on unknown properties of the structure might be patentable to the discoverer as a process of using. *In re Hack*, 245 F.2d 246, 248, 114 USPQ 161, 163 (CCPA 1957). However, when the claim recites using an old composition or structure and the "use" is directed to a result or property of that composition or structure, then the claim is anticipated. *In re May*, 574 F.2d 1082, 1090, 197 USPQ 601, 607 (CCPA 1978).

Thus while Baba *et al.* may not have been aware that the PEG-Chol composition was binding cholesterol, the PEG-Chol was nevertheless binding cholesterol and the detection by Baba *et al.* would serve both to determine and confirm the presence and distribution of the cholesterol in the living cells contacted with the PEG-Chol.

Baba *et al.* does not teach a method wherein the cells were contacted with up to 2 μM of labeled PEG-Chol or wherein the cholesterol detected is free cholesterol.

It would have been obvious to one of ordinary skill in the art at the time of the instant invention to modify the teachings of Baba *et al.* wherein living cells were contacted with PEG-Chol labeled with the affinity substance biotin (bPEG-Chol) by using the labeled PEG-Chol at a concentration of up to 2μM because the reference teaches the use of the PEG-Chol at a concentration of 2.5μM and the result-effective adjustment of conventional working parameters (e.g., determining an appropriate concentration of labeled PEG-Chol) is deemed merely a matter of judicious selection and routine optimization which is well within the purview of the skilled artisan.

Claims 3, 4, 9-11, 14, 15 and 19-21 are newly rejected under 35 U.S.C. 103(a) as being unpatentable over Baba *et al.* in view of Wu *et al.* (US 6,005,113).

The teachings of Baba *et al.* were discussed above.

Baba *et al.* does not teach a method wherein the detectable label is digoxigenin.

Wu *et al.* teaches the use of specific binding pairs such as biotin and digoxigenin, when allowed to react with their complementary specific binding pair member for the purposes of detection or quantitation (Column 13, Lines 16-25).

It would have been obvious to one of ordinary skill in the art at the time of the instant invention to modify the composition and *in vitro* labeling method comprising a polyethylene glycol cholesteryl ether (PEG-Chol) labeled with biotin as taught by Baba *et al.* above with the use of the digoxigenin as taught by Wu *et al.* because the specific binding pairs would have been recognized by one of ordinary skill in the art as functionally equivalent and the use of alternatives and functional equivalent techniques would have been desirable to those of ordinary skill in the art based upon the economics and availability of compounds and personal preference of the artisan. There would have been a reasonable expectation of success in making this modification because the method of Baba *et al.* taught the use of the biotin-fluorescent streptavidin specific binding pair and Wu *et al.* taught that biotin/digoxigenin were functional equivalents.

From the teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one of

ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

Response to Arguments

Applicant's arguments filed 10/12/07 have been fully considered but they are not persuasive.

The Applicant argues that Baba *et al.* does not disclose the contacting of up to 2.0μM of a labeled PEG-Chol with a living cell (Remarks, Pg. 24, Lines 1-8).

This is found to be persuasive and is addressed in the new rejection above.

The Applicant argues that Baba *et al.* does not disclose the various steps of the Applicant's process, presumably determining the presence and distribution of the labeled PEG-Chol bound to cholesterol, and confirming the presence and distribution of cholesterol in the living cell based upon the determining of the presence and distribution of labeled PEG-Chol bound to cholesterol (Remarks, Pg. 25, Lines 4-10).

This is not found to be persuasive for the reasoning cited in the rejection above, that the method of Baba *et al.* would inherently detect cholesterol in the living cells even though the reference may have been unaware that the PEG-Chol was binding to cell

surface cholesterol. By detecting and confirming the presence and distribution (See figures) of the PEG-Chol on the living cells, the reference was therefore inherently performing the detection, confirmation and distribution of cholesterol in the living cells.

The Applicant argues that Baba *et al.* discloses a phenomenon that PEG-Chol inhibits clathrin-independent endocytosis, an undefined mechanism (Remarks, Pg. 25, Lines 11-16).

This is not found to be persuasive as the rejection was based on whether or not the composition of Baba *et al.* is the same as instantly claimed and would function to bind to cholesterol.

The Applicant argues that Baba *et al.* uses PEG-Chol at a high concentration of 5-10mM which induces inhibition of clathrin-coated Endocytosis and thus detection of cholesterol in cells of normal state is impossible (Remarks, Pg. 25, Lines 17-21).

This is not found to be persuasive for the following reasons, as discussed above, Baba *et al.* teaches the use of labeled PEG-Chol at a wide range of concentrations, including at 2.5μM which barring any direct evidence to the contrary, is sufficiently close to the claimed value of 2μM as to be obvious to one of ordinary skill in the art.

The Applicant argues that it is an advantage over the prior art that the instant cholesterol detection agent can be used on living cells (Remarks, Pg. 26, Lines 4-7).

This is not found to be persuasive as no evidence has been presented that the composition and method of Baba *et al.* would not also inherently possess this "advantage".

Applicant's arguments with respect to claims 3, 4, 9-11, 14, 15 and 19-21 rejected under 35 U.S.C. § 103(a) as being unpatentable over Baba *et al.* (2001) in view of Wu *et al.* (US 6,005,113) have been considered but are moot in view of the new ground(s) of rejection above.

Conclusion

No Claims are allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Paul C. Martin whose telephone number is 571-272-3348. The examiner can normally be reached on M-F 8am-4:30pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jon Weber can be reached on 571-272-0925. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Paul Martin
Examiner
Art Unit 1657

12/13/07

JON WEBER
SUPERVISORY PATENT EXAMINER